

## CLAIMS

What is claimed is:

1. An antibody or antigen-binding fragment thereof, which binds to a mammalian GPR-9-6 and inhibits the binding of a ligand to said GPR-9-6.
2. The antibody or antigen-binding fragment of Claim 1 wherein said mammalian GPR-9-6 is human GPR-9-6.
3. The antibody or antigen-binding fragment of Claim 1 wherein said ligand is TECK.
4. The antibody or antigen-binding fragment of Claim 1 wherein the binding of said antibody or said antigen-binding fragment to GPR-9-6 can be inhibited by a peptide that consists of the amino acid sequence of SEQ ID NO:3.
5. The antibody or antigen-binding fragment of Claim 1 wherein the binding of said antibody or said antigen-binding fragment to GPR-9-6 can be inhibited by mAb 3C3.
6. The antibody or antigen-binding fragment of Claim 5 wherein said antibody or antigen binding fragment binds to the same or a similar epitope as mAb 3C3.
7. The antibody or antigen-binding fragment of Claim 1 wherein the binding of said antibody or said antigen-binding fragment to GPR-9-6 can be inhibited by mAb GPR96-1.

8. The antibody or antigen-binding fragment of Claim 7 wherein said antibody or antigen binding fragment binds to the same or a similar epitope as mAb GPR-9-6.

9. An antibody produced by murine hybridoma 3C3 or an antigen-binding fragment thereof.

10. An isolated cell which produces an antibody or antigen-binding fragment thereof which binds to a mammalian GPR-9-6 and inhibits the binding of a ligand to said GPR-9-6.

11. The isolated cell of Claim 10 wherein said mammalian GPR-9-6 is human GPR-9-6.

12. The isolated cell of Claim 11 wherein said ligand is TECK.

13. The isolated cell of Claim 12 wherein said isolated cell is selected from the group consisting of an immortalized B cell, a hybridoma and a recombinant cell comprising one or more exogenous nucleic acid molecules that encode said antibody or antigen-binding fragment thereof.

14. The murine hybridoma 3C3.

15. A method of detecting a mammalian GPR-9-6 or portion thereof in a biological sample, comprising:

5           a) contacting a biological sample with an antibody or antigen-binding fragment thereof which binds to a mammalian GPR-9-6 or portion of said receptor and inhibits binding of a ligand to the receptor, under conditions appropriate for binding of said antibody or antigen-binding fragment thereof to a mammalian GPR-9-6 or portion thereof; and

10           b) detecting binding of said antibody or antigen-binding fragment thereof, wherein the binding of said antibody or antigen-binding fragment thereof indicates the presence of said receptor or portion of said receptor.

16. The method according to Claim 15, wherein the biological sample is of human origin.

17. The method according to Claim 16, wherein the antibody or antigen-binding fragment thereof is selected from the group consisting of:

15           a) mAb 3C3;

              b) an antibody which can compete with mAb 3C3 for binding to a mammalian GPR-9-6;

              c) antigen-binding fragments of (a) or (b) which bind a mammalian GPR-9-6 or a portion thereof; and

20           d) combinations of the foregoing.

18. The method according to Claim 16, wherein the antibody or antigen-binding fragment thereof is selected from the group consisting of:

- mAb GPR96-1;
- an antibody which can compete with mAb GPR96-1 for binding to a mammalian GPR-9-6;
- antigen-binding fragments of (a) or (b) which bind a mammalian GPR-9-6 or a portion thereof; and
- combinations of the foregoing.

19. A method of detecting and identifying an agent which binds to a mammalian GPR-9-6 or a ligand binding variant thereof comprising combining:

- a reference agent;
- a test agent, and
- a composition comprising a functional mammalian GPR-9-6 or a ligand binding variant thereof under conditions suitable for binding of said reference agent to said GPR-9-6 or ligand-binding variant thereof; and detecting or measuring the formation of a complex between said reference agent and said GPR-9-6 or a ligand binding variant thereof, wherein, a decrease in the formation of said complex relative to a suitable control indicates that said test agent binds to said GPR-9-6 or to a ligand-binding variant thereof.

20. The method of Claim 19 wherein said reference agent is labeled with a label selected from the group consisting of a radioisotope, an epitope, an affinity label, an enzyme, a fluorescent group and a chemiluminescent group.

21. The method of Claim 19 wherein said reference agent is TECK.

22. The method of Claim 19 wherein said reference agent is an antibody which binds to said GPR-9-6 or an antigen-binding fragment thereof.

23. The method of Claim 19 wherein said composition comprising a functional mammalian GPR-9-6 or a ligand binding variant thereof is a cell that expresses a mammalian GPR-9-6.

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24. The method of Claim 23 wherein said cell is a recombinant cell.

25. The method of Claim 23 wherein said cell is a cell line.

26. The method of Claim 25 wherein said cell is selected from the group consisting of MOLT-4 and MOLT-13.

10 27. The method of Claim 19 wherein said composition comprising a functional mammalian GPR-9-6 or a ligand binding variant thereof is a membrane preparation of a cell that expresses a mammalian GPR-9-6 or a ligand binding variant thereof.

28. A method of detecting or identifying an inhibitor of a mammalian GPR-9-6 receptor comprising:

15 a) combining an agent to be tested, a ligand or promoter of said GPR-9-6 and a cell expressing said GPR-9-6 under conditions suitable for detecting a ligand- or promoter-induced response; and

b) determining the ability of the test compound to inhibit said response, wherein inhibition of a ligand- or promoter-induced response by the agent is indicative that the agent is an inhibitor.

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29. The method of Claim 28 wherein said cell is a recombinant cell expressing a human GPR-9-6.

30. The method of Claim 29 wherein said ligand or promoter is TECK.

31. The method of Claim 28 wherein said response is chemotaxis or  $\text{Ca}^{2+}$  flux.

5 32. A method of treating a subject having an inflammatory disease, comprising administering an effective amount of an antagonist of a mammalian GPR-9-6 function to said subject.

33. The method of Claim 32 wherein said inflammatory disease is Crohn's disease or colitis.

10 34. The method of Claim 32 wherein said antagonist inhibits the binding of a ligand to a mammalian GPR-9-6.

35. The method of Claim 34 wherein said ligand is TECK.

36. The method of Claim 34 wherein said antagonist is an antibody which binds to a mammalian GPR-9-6 or an antigen-binding fragment thereof.

15 37. A method of inhibiting GPR-9-6-mediated homing of leukocytes in a subject, comprising administering an effective amount of an antagonist of GPR-9-6 function to said subject.

38. The method of Claim 37 wherein said antagonist inhibits the binding of a ligand to GPR-9-6.

39. The method of Claim 38 wherein said ligand is TECK.

40. The method of Claim 39 wherein said antagonist is an antibody which binds to GPR-9-6 or an antigen-binding fragment thereof.

41. A method of inhibiting GPR-9-6-mediated homing of leukocytes to mucosal tissue in a subject, comprising administering an effective amount of an antagonist of GPR-9-6 function to said subject.

42. A method of treating a subject having an inflammatory bowel disease, comprising administering an effective amount of an antagonist of GPR-9-6 function to said subject.

10 43. The method of Claim 42 wherein said antagonist inhibits the binding of a ligand to GPR-9-6.

44. The method of Claim 43 wherein said ligand is TECK.

45. The method of Claim 44 wherein said antagonist is an antibody which binds to GPR-9-6 or an antigen-binding fragment thereof.

15 46. A method of modulating a GPR-9-6 function comprising contacting a cell that expresses GPR-9-6 with an agent which binds thereto, thereby modulating the function of said GPR-9-6.

47. The method of Claim 46 wherein said agent can inhibit a function of GPR-9-6.

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48. The method of Claim 47 wherein said agent is an antibody or antigen-binding fragment thereof.

49. The method of Claim 48 wherein said function is selected from the group consisting of ligand binding, ligand-induced chemotaxis and ligand-induced <sup>5</sup>  $\text{Ca}^{2+}$  flux.

50. The method of Claim 49 wherein said ligand is TECK.

51. A test kit for use in detecting the presence of a mammalian GPR-9-6 or portion thereof in a biological sample comprising

10 a) at least one antibody or antigen-binding fragment thereof which binds to a mammalian GPR-9-6 or portion of said receptor, wherein said antibody or antigen-binding fragment thereof inhibits binding of a ligand to the receptor; and

15 b) one or more ancillary reagents suitable for detecting the presence of a complex between said antibody or antigen-binding fragment thereof and said mammalian GPR-9-6 or a portion thereof.

52. A test kit according to Claim 51, wherein the antibody is selected from the group consisting of

20 a) mAb 3C3;

b) an antibody which can compete with mAb 3C3 for binding to mammalian GPR-9-6;

c) antigen-binding fragments of (a) or (b) which bind to mammalian GPR-9-6 or a portion thereof; and

d) combinations of the foregoing.

53. A test kit according to Claim 51, wherein the antibody is selected from the group consisting of

- mAb GPR96-1;
- an antibody which can compete with mAb GPR96-1 for binding to mammalian GPR-9-6;
- antigen-binding fragments of (a) or (b) which bind to mammalian GPR-9-6 or a portion thereof; and
- combinations of the foregoing.

54. An antibody or antigen-binding fragment thereof, which binds to a mammalian TECK and inhibits the binding of said TECK to a receptor.

55. The antibody or antigen-binding fragment of Claim 54 wherein said mammalian TECK is human TECK.

56. The antibody or antigen-binding fragment of Claim 54 wherein said receptor is GPR-9-6.

15 57. The antibody or antigen-binding fragment of Claim 54 wherein the binding of said antibody or said antigen-binding fragment to TECK can be inhibited by mAb 11.3.1 and/or mAb 16.3.1.

58. The antibody or antigen-binding fragment of Claim 57 wherein said antibody or antigen binding fragment binds to the same or a similar epitope as mAb 11.3.1.

20 59. The antibody or antigen-binding fragment of Claim 57 wherein said antibody or antigen binding fragment binds to the same or a similar epitope as mAb 16.3.1.

60. An antibody produced by murine hybridoma GPR96-1 or an antigen-binding fragment thereof.

61. The murine hybridoma GPR96-1.

62. An antibody produced by murine hybridoma 11.3.1 or an antigen-binding fragment thereof.

5 63. The murine hybridoma 11.3.1.

64. An antibody produced by murine hybridoma 16.3.1 or an antigen-binding fragment thereof.

65. The murine hybridoma 16.3.1.

10 66. An isolated cell which produces an antibody or antigen-binding fragment thereof which binds to a mammalian TECK and inhibits the binding of said TECK to a receptor.

67. The isolated cell of Claim 66 wherein said mammalian TECK is human TECK.

68. The isolated cell of Claim 66 wherein the receptor is GPR-9-6.

69. A method of detecting a mammalian TECK or portion thereof in a biological sample, comprising:

- a) contacting a biological sample with an antibody or antigen-binding fragment thereof which binds to a mammalian TECK or portion thereof and inhibits binding of a TECK to a receptor, under conditions appropriate for binding of said antibody or antigen-binding fragment thereof to a mammalian TECK or portion thereof; and
- b) detecting binding of said antibody or antigen-binding fragment thereof, wherein the binding of said antibody or antigen-binding fragment thereof indicates the presence of said receptor or portion of said receptor.

70. A test kit for use in detecting the presence of a mammalian TECK or portion thereof in a biological sample comprising

- a) at least one antibody or antigen-binding fragment thereof which binds to a mammalian TECK or portion of said receptor, wherein said antibody or antigen-binding fragment thereof inhibits binding of TECK to a receptor; and
- b) one or more ancillary reagents suitable for detecting the presence of a complex between said antibody or antigen-binding fragment thereof and said mammalian TECK or a portion thereof.

71. A method of treating a subject having cancer comprising administering to said subject an effective amount of an antagonist of GPR-9-6 function.

72. The method of Claim 62 wherein said antagonist is an antibody or antigen-binding fragment thereof which binds to GPR-9-6.

73. A method of treating a subject having cancer comprising administering to said subject an effective amount of an antibody which binds GPR-9-6 or an antigen-binding fragment thereof, wherein said antibody or fragment can activate complement.

5 74. A method of treating a subject having cancer comprising administering to said subject an effective amount of an immunoconjugate or antigen-binding fusion protein, wherein said immunoconjugate or antigen-binding fusion protein comprises at least an antigen-binding portion of an antibody which binds GPR-9-6 which is directly or indirectly bonded to an additional therapeutic agent.

10 75. The method of Claim 74 wherein said additional therapeutic agent is a cytotoxic agent.

76. An immunoconjugate comprising at least an antigen-binding portion of an antibody which binds GPR-9-6 which is directly or indirectly bonded to an additional therapeutic agent.

15 77. An antigen-binding fusion protein comprising at least an antigen-binding portion of an antibody which binds GPR-9-6 which is directly or indirectly bonded to an additional therapeutic agent, wherein said antigen-binding portion of an antibody and said additional therapeutic agent are part of a contiguous polypeptide.

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Ant B1  
Add C2